

Prevalence of HBsAg seropositivity during pregnancy and evaluation of vaccination programs: A multicenter study in Turkey

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ABSTRACT

OBJECTIVE: Hepatitis B virus (HBV) infection remains a global public health problem. Among its modes of transmission, vertical transmission from mother to child during pregnancy is exceedingly important. This study investigated seropositivity for hepatitis B surface antigen (HBsAg) among pregnant women aged 16–49 years and their pregnancy outcomes in several health institutions (university and state hospitals, family health centers) from seven cities in Turkey.

METHODS: An Excel form was sent to the sites participating in the study, and the total number of pregnant women who were tested for HBsAg between 2010 and 2017, HBsAg positivity rates, and the ages of HBsAg-positive pregnant women was collected retrospectively. Serum samples were obtained from 204,865 pregnant women from four regions between 2010 and 2017, including 107,463 from Black Sea, 2306 from Marmara, 48,339 from East Anatolia, and 46,757 from Aegean. HBsAg levels were determined on automated devices using chemiluminescence.

RESULTS: In the study, the data of 204,865 pregnant women from seven different provinces (Afyonkarahisar, Erzurum, Istanbul, Izmir, Manisa, Mus, and Rize) in different geographical regions were accessed, and HBsAg positivity was found in 2343 pregnant women (1.14%). The highest HBsAg seroprevalence was found in women who were older 26–40 years/1977–1991 birth year range on average. In the data of the present study, the number of pregnant women with HBsAg positivity among pregnant women born after the initiation of the national vaccination program and catch-up vaccination program is only 124 and constitutes 5.3% of all HBsAg-positive pregnant women

CONCLUSION: In this study, it has been found that HBsAg positivity in pregnant women has been decreasing in Turkey and that it is significantly lower, especially in those born after the initiation of the national vaccination program. Continuation of national neonatal HBV vaccination with high compliance is very important.

Keywords: HBsAg; pregnancy; seropositivity.

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Hepatitis B virus (HBV) is a microorganism that causes acute and chronic hepatitis, cirrhosis, and hepatocellular carcinoma [1]. Despite having an effective and safe vaccine, approximately 257 million people around the world are diagnosed with the disease, and nearly 600,000 people/year lose their lives due to acute or chronic HBV infection, indicating the importance of this microorganism [2]. The possibility of infection with HBV becoming chronic is inversely proportional to the age the virus is acquired [3, 4]. An important source of the spread of HBV is women in the reproductive age group with chronic HBV infection.

Many international organizations (Advisory Committee on Immunization Practices, World Health Organization) recommend that all pregnant women be tested for hepatitis B surface antigen (HBsAg). Even though vaccine + immune globin has been administered to the infant against HBV for many years, perinatal transmission occurs in at least in 10% of children born to mothers with high levels of viremia [5, 6]. For this reason, oral antiviral use in the last trimester has been recommended in some pregnant women in recent years [7, 8].

This study aimed to determine the current status HBsAg seropositivity in pregnant women in different regions in our country, which is important to know for the management of HBV infection during pregnancy and prevention of vertical transmission.

MATERIALS AND METHODS

Patients

In this multicenter study, records of 204,865 pregnant women aged of 16–49 years who applied to state health institutions and who were living in urban and rural parts of seven cities (Afyonkarahisar, Erzurum, Istanbul, Izmir, Manisa, Muş, and Rize) in different regions of Turkey between 2010 and 2017 (the first 4 months of 2017) were retrospectively reviewed. Serum samples were obtained from 204,865 pregnant women from four regions between 2010 and 2017, including 107,463 from Black Sea, 2306 from Marmara, 48,339 from East Anatolia, and 46,757 from Aegean. In order not to use repetitive data of pregnant women, only a single HBsAg result of each pregnant woman with HBsAg positivity was taken into evaluation. The provinces that participated in the study and the number of pregnant women who were tested for HBsAg were as follows in alphabetical order: Afyonkarahisar 4725, Erzurum 36,123, İstanbul 2306, İzmir 6038, Manisa 35,994, Muş 12,216, and Rize 107,463.

Highlight key points

- Monitoring of seropositivity rates for HBsAg very important among pregnant women.
- Thanks to national HBV vaccination program, HBsAg positivity in pregnant women has been decreasing in Turkey.
- Preventing vertical transmission is very important.

Immunochemistry

Tests were performed in each hospital's own microbiology laboratory, and each hospital identified HBsAg-positive cases according to the reference intervals of its own laboratory. These data were collected retrospectively.

Ethics

Before collecting data, ethics committee approval for this multicenter study was obtained from the Non-interventional Clinical Research Ethics Committee of University of Health Sciences, Izmir Bozyaka Training and Research Hospital (2016/430) and the Ministry of Public Health Institution of Turkey.

Statistical Analysis

Statistical analysis of all data was performed using the JASP (open-source statistic program) program. Results are presented as percentage and number for categorical variables and mean \pm standard deviation or median (minimum [min]-maximum [max]) for continuous variables. Chi-square and Fisher's exact test were utilized for the comparison of group rates. $P < 0.05$ was considered statistically significant.

RESULTS

Among the 204,865 pregnant women tested, 2343 (1.14%) were HBsAg positive (Table 1). HBsAg positivity rates by years are shown in Table 1, and there was no statistically significant difference between the years.

Distribution of pregnant women with HBsAg positivity by their years of birth is shown in Table 2. The results have been given with reference to years of birth. When the distribution by age groups was analyzed, the lowest rate was found in the period after the initiation of the national HBV vaccination in Turkey ($p < 0.05$). It has been determined that HBsAg positivity increases with age ($p < 0.05$). The highest HBsAg seroprevalence was found in women who were older 26–40 years/1977–1991 birth year range on average.

TABLE 1. Distribution of HBsAg-positive pregnant women by years

Year	HBsAg positive n (%)	Total n
2010	287 (1.16)	24593
2011	84 (0.61)	13645
2012	407 (1.34)	30357
2013	347 (1.29)	26860
2014	343 (1.01)	33728
2015	273 (0.90)	30120
2016	479 (1.27)	37429
2017*	123 (1.51)	8133
Total	2343 (1.14)	204.865

*: The first 4 months; HBsAg: Hepatitis B surface antigen.

Distribution of pregnant women with HBsAg positivity by provinces (geographical regions) is shown in Table 3. There was a marked difference in seroprevalence by region, ranging from 0.6% (Rize) to 2.4% (Mus). Aegean and Marmara regions which are regions west of the Turkey and low HBsAg positivity. East Anatolia region of Turkey is located east of the country and HBsAg positivity is high. Black Sea region has mild endemicity for HBsAg. It has been observed that the number of HBsAg-positive pregnant women is higher in the province of Muş located in the East Anatolia region, followed by Manisa, which is located in the west but is a province that receives migration from East and Southeast provinces.

DISCUSSION

HBV infection can be prevented by safe and effective vaccine [9]. Hepatitis B vaccine prevents HBV infection in both children and adults. In infants, the hepatitis B vaccine and hepatitis B immunoglobulin have been shown to be 90–95% effective in preventing perinatal HBV infection if it is administered within 24 h of birth followed by at least two more doses [10, 11]. Yet, in 2014, <38% of the newborns in the world had HBV vaccine administered within 24 h after birth [12].

Given the danger of vertical transmission to a baby from a mother who is HBsAg positive, evaluating HBV status in pregnant women is critically important [7, 8, 13]. Before the implementation of vaccination programs, the prevalence of HBsAg among adults was below 2% in Europe and North America, whereas it was 15–20%

TABLE 2. Age groups of HBsAg-positive pregnant women and distribution by birth dates

Age groups (by years)	Age groups (by ages)	% n=2343
2000–1997	17–20	5.30
1996–1992	21–25	16.81
1991–1987	26–30	22.40
1986–1982	31–35	26.70
1981–1977	36–40	18.43
1976–1972	41–45	8.20
1971 and before	46+	2.20

HBsAg: Hepatitis B surface antigen.

TABLE 3. Distribution of HBsAg-positive pregnant women by provinces (in alphabetical order)

Provinces	Geographic area	HBsAg- positive pregnant women (n=2343)	Total number (n=204,865)	%
Afyon	Aegean	71	4725	1.5
Erzurum	East Anatolia	481	36,123	1.3
Istanbul	Marmara	37	2306	1.6
Izmir	Aegean	103	6038	1.7
Manisa	Aegean	692	35,994	1.9
Mus	East Anatolia	304	12,216	2.4
Rize	Black sea	655	107,463	0.6

HBsAg: Hepatitis B surface antigen.

in most Asian and European countries [14]. It was reported that the transmission route of new infections was parenteral and sexual in Europe and North America, however, it was known that transmission from infected mother to the baby continued in the hyperendemic regions [15]. Maternal screening for HBV and implementation of anti-transmission programs to reduce maternal transmission and the population of HBV carriers are, therefore, very important in hyperendemic areas. Results of national immunoprophylactic vaccine applications for HBV have been positive worldwide. HBV infection in Taiwan was hyperendemic until the 1990s. In Taiwan, where universal vaccination in childhood practices was carried out meticulously, before universal HBV vaccina-

tion was initiated in 1984, the carrier rate for HBsAg was 15–20% in the general population [16].

In a study from Taiwan evaluating the effectiveness of its vaccination program, the chronic HBV infection rate was lowered from 10% to 1% among children over 10 years by testing pregnant women and immunizing newborns [17]. In the same population, the rate of hepatocellular carcinoma in children 6–14 years old was reduced from 0.7–0.36/100,000 [18].

Turkey is considered an intermediate endemic area for HBV by the World Health Organization [14, 19]. Seroprevalence of HBsAg was found to be 4% in the studies conducted on the general population in Turkey and it was reported that this rate varies between the regions and that the prevalence of HBV increases from the west to the east [20]. Epidemiologic studies conducted in the past two decades reveal a rate of HBsAg seropositivity among the general Turkish population between 4% and 5%. However, there are regional differences in the prevalence [20–22]. The TURHEP study reported HBsAg seropositivity of 4% in the general population, 2.3% in the Aegean region, 6.1% in the Black Sea region, 4.3% in Central Anatolia, 3.4% in East Anatolia, 3.8% in the Marmara region, 3.1% in the Mediterranean region, and 7.3% in Southeast Anatolia [22].

HBsAg positivity in pregnant women in Turkey in the years 1987–2004 was reported to be between 3.5% and 9.3% [23]. In a review of studies covering pregnant women in Turkey, a total of 64 studies conducted between 1975 and 2016 were reviewed. In these studies, HBsAg positivity rates in pregnant women were found to be between 1.2% and 19.2%, and it was emphasized that HBsAg positivity had decreased in recent years [20, 24].

A study retrospectively examined the test results of pregnant women who presented to the University Hospital between 2012 and 2014 in Zonguldak, a province in the Black Sea Region, and found an HBsAg positivity rate of 4% and an anti-HBs positivity rate of 7.3% in a total of 1084 pregnant women with a mean age of 29 years [25].

In another retrospective study conducted in Turkey, the rates of HBsAg and anti-HBs in pregnant women who were monitored at four centers between 1995 and 2015 were examined. When the results were evaluated, HBsAg positivity was found to be 1.5%, and anti-HBs positivity was found to be 11.5% [26].

When the change in these results by years was examined, HBsAg positivity was 2.6% ($n=3010$) between 1995 and 2001, 0.8% ($n=2995$) between 2002 and 2008, and 0.8% ($n=1600$) between 2009 and 2015, while an-

ti-HBs positivity rates were 9.5%, 10.3%, and 17.5%, respectively. Furthermore, in the present study, it has been found that HBsAg positivity has decreased in pregnant women over the years.

In this study, when the age distribution of 2343 HBsAg-positive pregnant women was examined, it was found that the highest rate of HBsAg positivity was between 26–35 and 36–40 age groups.

All newborn babies in Turkey since 1998 have been vaccinated at birth, with subsequent injections according to the standard schedule as a part of National Immunization Programme. Then, by applying National catch-up HBV vaccination program, adolescent vaccination was performed and those born in 1996 and before were vaccinated with three doses.

According to the Ministry of Health, the incidence of hepatitis B infection in 2002 was 8.26/100,000 persons, but it had dropped to 4.26 in 2010 [27]. In an article evaluating the universal HBV vaccination program in Turkey, it was emphasized that there was a significant decrease in the number of HBV infections, especially under the age of 15 in the period between 1990 and 2012 as a result of the prevention and protection strategies [28]. In the data of the present study, the number of pregnant women with HBsAg positivity among pregnant women born after the initiation of the national vaccination program and catch-up vaccination program is only 124 and constitutes 5.3% of all HBsAg-positive pregnant women. The number and rate of HBsAg-positive pregnant women increase with age, and low rates at the age of 41 and above are considered to be related to the low number of pregnant women in that age group. When the distribution by geographical regions was examined, it was found that HBsAg positivity was high (2.4%) in pregnant women in the province of Muş in the East Anatolia region, a region where HBsAg positivity is high. This is followed by the province of Manisa with a rate of 1.9%. Although the province of Manisa is located in the west of Turkey, it is a province that receives intense migration from regions where HBV infection is endemic, such as the East and Southeast Anatolia regions, due to the high number of industrial workplaces, and this may be associated with the high result [29].

Limitations of the Study

Since the study was conducted retrospectively and on a voluntary basis, participation from all geographical regions of Turkey could not be achieved. In addition, as it is difficult to access retrospective data, only a single

result of the pregnant women who were found to have HBsAg positivity was evaluated in order not to use repetitive data of the same pregnant women and to avoid bias related to this issue. Therefore, since the data of HBsAg-negative pregnant women could not be accessed for every age group, the percentage within each age group could not be calculated. However, we believe that the data of the present study would be significant since there were participants from different provinces in Turkey, and a high number of cases in a recent period of 7 years were included in the study.

The rates of HBsAg testing in pregnant women are lower throughout Turkey since there was no legal obligation for testing until last year. However, we believe that awareness on this issue and therefore rates of HBsAg testing during pregnancy will increase through the “Turkey Viral Hepatitis Prevention and Control Program (2018–2023)” that was put into force in October 2018 [30].

As a result, testing for HBsAg seropositivity is important in the general population, as failing to identify those who are chronically infected may mean that they have no opportunity to be treated before they develop chronic hepatitis or hepatocellular carcinoma. However, seropositivity in pregnant women poses a risk not only for themselves but also for their babies. Therefore, health services should be accessible and regularly provided so that pregnant women in all areas of the country are appropriately tested and followed. It is important to include the foreign immigrant population in testing schemes.

Conclusion

In this study, we have found that HBsAg positivity in pregnant women has been decreasing gradually and that it has been significantly lower, especially in those born after the initiation of the national vaccination program in Turkey. We believe that our study provides useful data about the current epidemiology of hepatitis B infection in pregnant women in Turkey that will be of use in health planning. We would like to emphasize once again that it is very important to continue with the national neonatal HBV vaccination program with high compliance and to test for HBsAg in all pregnant women for the continuation of this achievement.

Ethics Committee Approval: Ethics committee approval for multi-centered study was taken from Non-interventional Clinical Research Ethic Committee of Izmir Bozyaka Training and Research Hospital, Health Sciences University (2016/430) and Public Health Institution of Turkey.

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